GLOBAL INFLUENZA PROGRAMME

World Health Organization

REPORT OF THE WHO CONSULTATION ON SURVEILLANCE FOR PANDEMIC INFLUENZA

GENEVA, SWITZERLAND

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Geneva, Switzerland
10-12 December 2007

World Health Organization

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1. Background

In the 40 years since the 1968–1969 H3N2 influenza pandemic, substantial societal and public health changes have occurred. Many of these changes are expected to affect the emergence, spread and control of the next pandemic. For example, people travel more widely, more frequently and to more remote areas using increasingly faster modes of transportation. This increased global "connectivity" and interdependency of societal systems will most likely contribute to the accelerated global spread of a new pandemic virus. The rapidity with which a novel virus can circumnavigate the globe was amply demonstrated by the Severe Acute Respiratory Syndrome (SARS) experience of 2003; on the other hand, SARS also demonstrated that it is possible to use modern technology to mount a complex public health response.

Today, the global public health community has new and improved tools to help prepare for and respond to a pandemic that were not available in 1968–69. These include antiviral drugs and nascent technologies to speed the development of pandemic vaccines; improved molecular and genetic techniques to analyse and track the evolution of influenza viruses; and mathematical methods to model the evolution and spread of a pandemic virus, estimate incidence and prevalence and assess the impact of pharmaceutical and non-pharmaceutical measures on disease transmission and associated morbidity and mortality.

The intervening decade since the first emergence in 1997 of avian influenza A (H5N1) has given the world an unprecedented opportunity to prepare for a possible pandemic. The World Health Organization (WHO) has developed a protocol outlining how the first emergence of a pandemic virus might be rapidly contained before it has spread widely. Most countries have developed pandemic preparedness plans; some national plans include the integration of government and non-government sectors. Many countries are considering how best to implement various public health measures during a pandemic and some have strategic stockpiles of antibiotics, antivirals, human H5N1 influenza vaccine and personal protective equipment. Importantly, the International Health Regulations (2005) have come into force. They include key provisions for surveillance and notification to WHO of "events which may constitute a public health emergency of international concern",[1] such as cases of a new subtype of influenza.

Epidemiological surveillance at the global level can help countries anticipate a pandemic's impact and guide their response as the pandemic evolves. Systems exist at global and national levels to monitor seasonal influenza and detect the emergence of influenza viruses with pandemic potential. These systems, however, have not been designed to cope with a pandemic situation where tens of millions of people are infected over a very short period of time.

The heterogeneous nature of influenza surveillance is an additional challenge. In some countries, infectious disease and/or influenza surveillance systems barely exist (if at all), while at the other end of the spectrum are countries with multiple and sophisticated systems. Systems can be laboratory-, disease- or syndrome-based; some are integrated, some generic and others are influenza-specific. Electronic tools for data collection and transmittal are increasingly being used, although many systems remain relatively set by a variety of factors with limited flexibility.

Against this backdrop, policy-makers, the media and the public have high expectations that public health organizations will respond swiftly, efficiently and effectively once a pandemic begins. Surveillance data will be essential to inform the public health response at local, national and global levels.

[1] *International health regulations (2005),* 2nd ed. Geneva, World Health Organization, 2008.

2. The consultation

With a view to addressing the above expectations, WHO convened a technical consultation on surveillance for pandemic influenza from 10 to 12 December 2007. The consultation, attended by 97 experts and key stakeholders from 25 countries, considered what information would be needed during a pandemic, whether existing surveillance systems would be capable of collecting this information, and ways to analyse and disseminate key information during a pandemic. The programme and list of participants of the consultation can be found in Annexes 1 and 2 respectively. The outcome of the consultation will inform a working group that will develop guidelines for pandemic influenza surveillance at the global level. The consultation was part of a series of interrelated consultations held in 2007 and 2008 to address various aspects of pandemic preparedness, including an update and revision of the 2005 WHO global influenza preparedness plan and a consultation on disease control measures during a pandemic.

The objectives of the consultation were:

1. to determine the core information that should be gathered by WHO to help Member States monitor and manage a pandemic situation at national level;
2. to identify approaches and tools for WHO to receive data from Member States, and to analyse and disseminate the information in a timely manner;
3. to identify essential next steps to produce the guidelines and improve global disease surveillance during a pandemic.

3. Lessons and opportunities identified from relevant experiences

Summary points:

- Advance planning is critical to specify what information should be collected during a pandemic and how data will be managed, analysed and shared at the global level.
- Some information will be used in real time and some will be analysed after the pandemic.
- Information will come from multiple sources, and analysis and interpretation may not be straightforward. Global-level working groups with relevant expertise should be used to strengthen the analysis process.

There are few examples of public health responses that compare to the scale and magnitude of a pandemic. Experience from previous pandemics highlight gaps in knowledge and the need to develop more systematic approaches to data collection. The global response to SARS included new approaches to surveillance and strategic partnerships that can be adapted for an influenza pandemic.

Previous influenza pandemics:
Information about previous pandemics can be obtained from international media reports published at the time, public health reports written soon after the event and retrospective analyses. Using these sources, it is possible to derive

information on etiology and virological subtype, transmission, attack rates, case fatality rates, serial intervals, effective reproductive numbers (R_o), epidemic curves, and who and which community functions were affected. A consistent finding, as illustrated by data from the United Kingdom (UK), was local variation in mortality rates during a pandemic.

Little of this information was known even during the last pandemic in 1968–69. Some of the key information gaps that remain today are an understanding of the dynamics of the disease, how it spreads and the effectiveness of various interventions such as masks, school closures, movement restrictions and border closures.

SARS:
The global public health response to SARS in 2003, including surveillance and reporting of cases, is probably the closest experience to an influenza pandemic in modern times. During the outbreak, WHO provided guidance on surveillance for the new disease and collected and disseminated global surveillance data. A minimum global dataset was specified to support monitoring, risk assessment, decision-making and evaluation needs. Practical aspects of surveillance included provision of a data dictionary and clear instructions about the frequency and methods of reporting.

WHO and some countries found it helpful to identify separate operational and decision-support teams. The former (called Team A) was immersed in the day-to-day operations to collate, analyse and track the epidemic. The latter (called Team B) functioned at "arm's length" to review and reflect on surveillance data and other information, pose questions to facilitate evaluation and lend support for decision-making.

The rapidly evolving situation, complicated by multiple stakeholders with varying information needs, required open and transparent access to data. However, this raised complex ethical and data ownership issues for both WHO (as custodian of the global data) and countries that were not easily resolved. Development of a well-nuanced data sharing plan in advance of a pandemic is strongly advised to specify what level of data will be shared and how it can be used.

During the SARS outbreak, WHO formed several "virtual" working groups including the SARS Epidemiology Working Group. This Group of laboratory experts met regularly by teleconference to exchange information and data in real time, review guidance documents drafted by WHO and national public health agencies and serve as a problem solving resource for WHO. Their teleconferences and meeting minutes were also shared with the Clinical Working Group. The Epidemiology Working Group also prepared a consensus document on the epidemiology of SARS. Communication within the Group was facilitated by a secure web site; in the future collaborative electronic work spaces may serve as an additional resource to share preliminary information, assist in rumour alert and verification and host on-line discussions.

4. Expectations and perspectives of countries and the media

Summary points:

Pandemic influenza surveillance at the global level must consider:

- what data to collect in order to assess and monitor key parameters over time;
- different ways to collect data such as special studies, routine surveillance and the use of sentinel sites;
- processes to ensure data quality and reliability;
- how to provide the best information available in a timely and easily understood format;

- how frequently information should be updated; and
- changing information needs over the course of the pandemic.

Member States and the media are among the key partners and stakeholders whose perspectives can help inform the development of a plan for global pandemic influenza surveillance.

Member Sates:

Irrespective of their country's level of resources and development, consultation participants consistently voiced high expectations about what information WHO should provide at the global level during a pandemic (see annexes 3 and 4). Participants indicated that the following information would help them address national concerns such as morbidity, mortality and social disruption as well as anticipate needs in health care and other sectors in the allocation of scarce resources:

- epidemiological, clinical and virological parameters of the pandemic virus;
- pharmaceutical (antivirals and vaccines) and non-pharmaceutical interventions;
- details on the global spread of the disease;
- surveillance and case definitions; and
- triggers to start and stop interventions.

It was agreed that priorities related to data collection and analysis will change during the pandemic and this needs to be taken into consideration when planning for pandemic surveillance at national and global levels. While the pandemic is under way, information will be urgently needed for immediate action, e.g. on the severity of the disease and how many additional treatment centres are needed. Other information collected during the pandemic could be analysed after termination of the pandemic, e.g. the number of patients who received a complete course of antiviral therapy. These changing information needs (Figure 1) will require different types of data collection approaches, including detailed case investigations or special studies linked to outbreaks early in the pandemic, and traditional disease surveillance for "core" data during the pandemic. The discussion raised questions about how information would be collected, shared with WHO

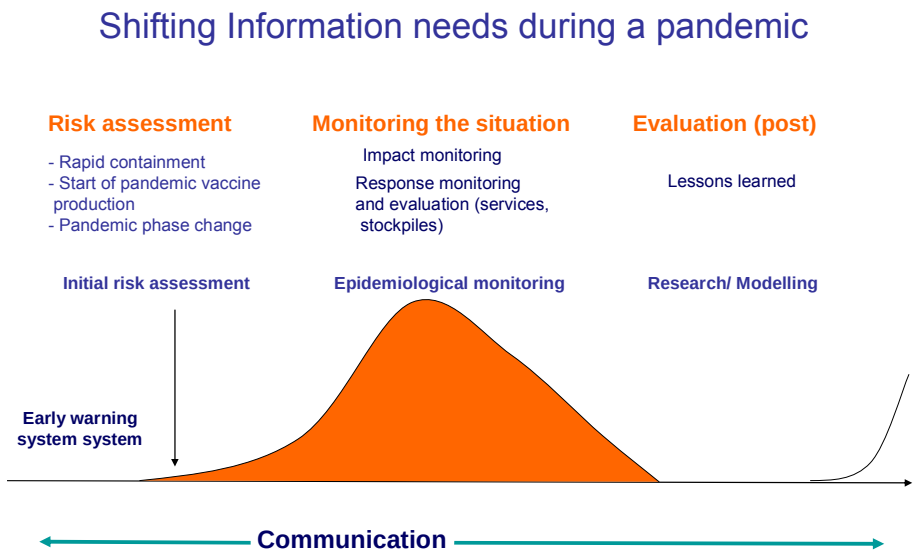

Fig. 1: Changing information needs during a pandemic

and aggregated at the global level. It was also noted that the quality of data was likely to vary and such limitations needed to be acknowledged.

To cope with the overwhelming amount of information that a pandemic would generate, participants stressed the importance of establishing a process whereby data could be carefully sifted and synthesized to best inform and guide public health action.

Practical suggestions for WHO included daily or twice daily briefings (in view of different global time zones) and pre-notification to Member States before official announcements to other Member States and/or public. If possible. Information sharing should be open and transparent.

Challenges for pandemic surveillance in resource-poor countries are particularly acute and include a low level of commitment by policy-makers and partners; little capacity for collection, collation, analysis and timely reporting of surveillance data; inadequate laboratory resources, notably basic equipment, supplies, facilities and trained staff; lack of systems for seasonal influenza surveillance; and inadequate logistics support and training.

The media:

An influenza pandemic will generate considerable demand for accurate and timely information from many parties including WHO, countries, politicians, the media, scientists, public health officials, modellers, the business community and the general public. Although there will be no shortage of information, much of it will be confusing and at times inaccurate depending on the source and quality of the data, as well as the expertise and knowledge of the spokesperson. The media will certainly access global, regional and national surveillance data. However, other types of information will be sought such as the impact of the pandemic on the economy, schools, transit, travel and health care, and the availability of antivirals, personal protective equipment and other supplies.

Important work can be undertaken in advance of the pandemic such as simulation exercises. In addition, all stakeholders should be advised to expect uncertainty and incomplete information, especially during the early stages of a pandemic. WHO reports should serve as a credible, stabilizing source of information and guidance.

5. Review of existing surveillance systems:

Summary points:

- Surveillance systems span a spectrum of complexity, methods and resources. Modifying existing systems will be necessary to meet the demands of a pandemic.
- Pandemic surveillance will not be done in a uniform way and global pandemic surveillance will integrate data from heterogeneous national, regional and global systems.
- The challenge is to define both the minimum data to be shared at global level on a routine basis and the more detailed data to be collected by a subset of countries.
- Advance planning, practical guidance and simple systems that accommodate varying levels of infrastructure and capacity can maximize the number of countries participating in a global surveillance system.

5.1 Examples of global-level systems

Two WHO systems collect influenza surveillance data at the global level: the Global Influenza Surveillance Network (GISN) with FluNet as data reporting system and an early warning system.

The GISN is a network of laboratories involved in virological surveillance. It plays a significant role in supporting WHO's recommendations on influenza vaccine composition. The GISN comprises 118 National Influenza Centres (NICs) in 89 countries, four WHO Collaborating Centres (CC) for Reference and Research on Influenza, three key national reference laboratories involved in vaccine virus selection and development, and a WHO Collaborating Centre for Studies on the Ecology of Influenza in Animals (FiG. 2). NICs collect specimens in their country and perform primary virus isolation and preliminary antigenic characterization. They ship newly isolated strains to WHO CCs for more sophisticated antigenic and genetic analysis, the results of which form the basis of WHO recommendations on the composition of influenza vaccine for the northern and southern hemispheres each year. In addition, the GISN updates seasonal influenza diagnostic reagents and monitors antiviral susceptibility. As at 2008, only minimal epidemiological information was reported to the GISN.

Created in 1995 with data from 78 countries, FluNet is a web-based interactive data reporting, query and mapping system for support and coordination of national and global influenza surveillance. Currently, 83 NICs contribute to FluNet. It facilitates real-time monitoring of influenza activity around the world and includes information about influenza-like illness (ILI) activity and the number of isolates and specimens processed.

The GISN also has an important role in monitoring and assessing the potential risk that influenza A (H5N1) and other viruses pose for a pandemic. GISN laboratories perform detailed molecular and antigenic analyses of H5N1 isolates, identify H5N1 human viruses suitable for vaccine development, develop and update diagnostic reagents and protocols for human infections, provide confirmatory diagnostic services, assist in outbreak investigations and monitor antiviral susceptibility.

The second WHO global surveillance system is for early warnings. This system screens daily reports from the media using tools as Global Public Health Intelligence Network (GPHIN) and reports from formal and informal networks on events of potential global public health importance such as H5N1 infections or other influenza

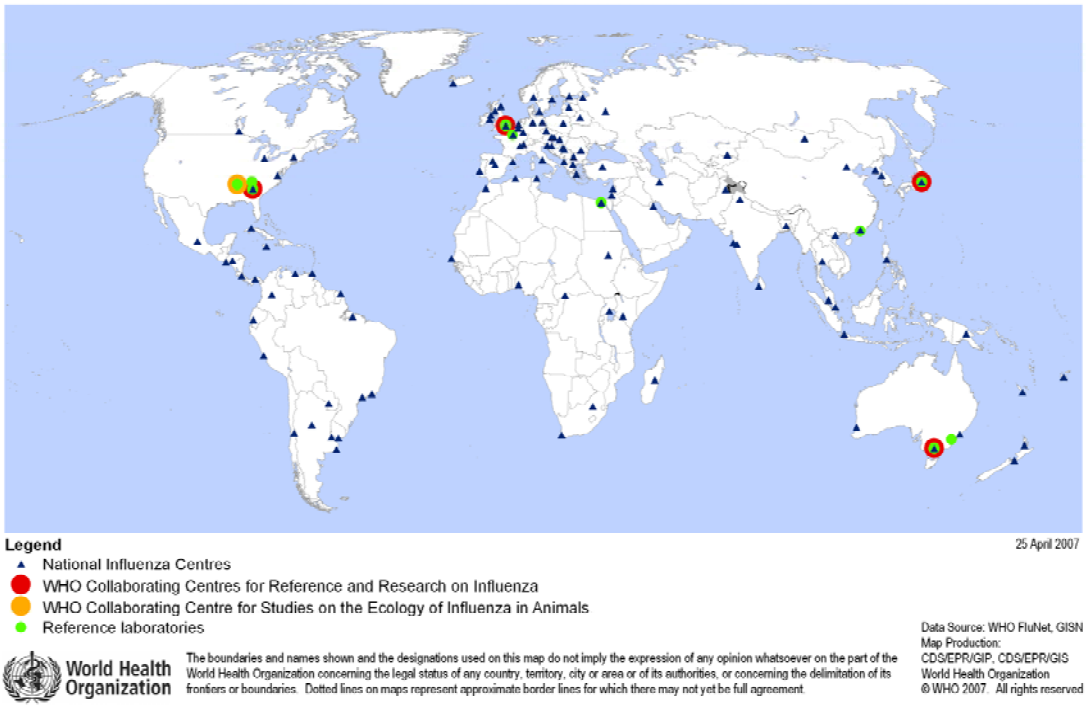

Fig. 2: WHO National Influenza Centres, Collaborating Centres and Reference Laboratories 2007

viruses with pandemic potential. Efforts to verify unsubstantiated reports and rumours can include an epidemiological investigation if required. WHO's Global Alert and Response Network (GOARN), comprising 114 international organizations and partners, can provide expertise to carry out epidemiological investigations and support for rapid containment of an emerging pandemic.

WHO has long-established systems for virological surveillance of seasonal and novel influenza; however, it does not have a comparable system to collect epidemiological and virological data during a pandemic. The early warning system will be instrumental at the beginning of a pandemic but may well not be adequate for sustained surveillance until the termination of a pandemic.

5.2 Examples of regional-level systems

At the regional level, two interesting examples illustrate the challenges of integrating national sources of data. These are the European Influenza Surveillance Scheme (EISS), a surveillance system with both virological and epidemiological components, and the Integrated Disease Surveillance (IDS) system, an early warning system focused on rapid detection of epidemic diseases in Africa.

EISS comprises 35 member countries and a population base of 498 million persons. Both virological and epidemiological data are collected and reported using a web-based platform. Virological data are supplied by national reference laboratories that receive specimens from general practitioners (GPs), hospitals and other sources. EISS hosts the Community Network of Reference Laboratories for Human Influenza in Europe (CNRL). Epidemiological data, including age-specific community data, are collected by a network of 25 750 sentinel physicians who also supply community-based specimens for analysis. Each week data are processed over three days and published in an electronic bulletin.[2] The system requires six to seven persons to operate but could function with fewer. It offers several advantages including an enhanced database and harmonized key surveillance indicators such as age groups and laboratory activities despite differing health systems across Europe. Areas for improvement are further harmonization (e.g. a common definition for reporting of ILI), inclusion of cases that do not seek care from GPs and a mechanism to share regional data with modellers. EISS will operate out of the European Centre for Disease Prevention and Control (ECDC) as from September 2008 and will serve as the base for pandemic surveillance in Europe.

IDS is a regional strategy to provide timely data for decision-making and public health interventions to control 19 priority communicable diseases. Recently it has evolved to include events specified under the IHR (2005). The system relies on the use of simple case definitions, collection of minimal information, integration of reporting forms and provision of feedback. Reporting frequency ranges from real-time case-based/line listing information to weekly, monthly and quarterly aggregated data. Case-based information includes name, age, sex, address, location (urban/rural), date of onset/admission, laboratory result, diagnosis and outcome. Aggregated data (i.e. number of cases and deaths) are age-stratified as < 5 years and ≥ 5 years. Although IDS has helped improve epidemic detection and response capacities, progress has been slow; it required 10 years for 43 countries to implement the system. Influenza-specific surveillance is not carried out in many countries in the African region and there are only nine NICs in eight countries in this region. Enhanced surveillance for H5N1 within IDS includes "zero reporting" carried out currently by 23 countries, coordination with animal surveillance, and

[2] http://www.eiss.org/cgi-files/bulletin_v2.cgi?season=2008 accessed on 19 December 2008

rumour/event verification. Some countries in the region are planning to implement severe acute respiratory illness (SARI)/ILI surveillance through bilateral cooperative agreements with the US Centers for Disease Control and Prevention (CDC).

Pandemic influenza surveillance in the African region could theoretically follow the IDS model, i.e. collection of case-based data for the first 100–200 cases per country (as is done for meningococcal disease) followed by a move to reporting aggregated data (cases/deaths) and the number of countries/provinces/districts affected on a daily or weekly basis. Nonetheless, many challenges can be anticipated for IDS-based pandemic influenza surveillance, for instance the timeliness of reporting (related in part to the time required for information to flow from the Ministry of Health to WHO Country and Regional Offices and then Headquarters), incomplete information, data quality issues, communication failures and lack of resources.

During the discussion it was noted that the WHO Regional Office for the Americas and CDC have developed a generic protocol for influenza surveillance that integrates epidemiological and laboratory components. The protocol outlines a two-pronged approach: a sentinel surveillance system for ILI in outpatients and SARI and SARI-related mortality in hospital patients coupled with an enhanced nationwide notifiable disease surveillance system for unusual occurrences of acute respiratory infections. PAHO plans to implement the protocol on a pilot basis in 2008. The difficulty of introducing standardized methodology in areas with pre-existing systems was noted.

5.3 Examples of country-level systems

To participate in global surveillance for pandemic influenza, countries need a surveillance system that is able to gather the required data. Three types of country-level surveillance systems were reviewed:

- Long-standing seasonal influenza surveillance systems with both virological and disease components. During a pandemic, such systems can serve as a foundation upon which new components can be added or existing components restructured.
- Sentinel surveillance or early warning systems in community and hospital settings to detect human cases of infection with H5N1 or other novel influenza virus strains that may signal the start of a pandemic.
- Surveillance systems for diseases such as polio that could be used during a pandemic with some adaptation.

Countries without pre-existing surveillance systems when a pandemic starts may be able to implement an ad hoc system modelled on approaches used during “chaotic situations.”

Long-standing influenza surveillance systems:

Canada, France, Japan and the UK described their current seasonal influenza programmes. All four countries rely on a multi-component strategy that typically includes (i) assessment of morbidity through sentinel physicians and hospital networks; (ii) virological surveillance; and (iii) mortality data (with the exception of Canada which is piloting population-based severity/mortality surveillance during 2007–08). Data are reported as influenza rates per population. Other country-specific components include school absenteeism (Japan), “cold/flu/fever” calls to a 24/7 nurse-led clinical helpline (UK), hospital bed activity (UK), provincial-level qualitative influenza “activity” (Canada), outbreak reporting (UK) and surveillance for hospitalized severe cases (Canada and France [paediatric only]).

Canada, Japan and the UK described plans to adapt their seasonal systems to a pandemic situation. During the pre-pandemic period, or at the initial occurrence of pandemic influenza, each of the three countries plans to collect more detailed case- or cluster-

based data such as clinical characteristics and course, transmission patterns, response to antivirals, virus characterization and antiviral susceptibility testing. The Netherlands plans to undertake a multidisciplinary systematic follow-up of early cases and their contacts using a unified database, and to conduct seroprevalence surveys in existing serodatabases. The ECDC is exploring the possibility of using the UK's enhanced web-based reporting system for detailed data collection throughout Europe. This enhanced data collection would continue for a limited period of time (e.g. covering the first few hundred cases as in the UK).

Over the course of the pandemic Japan plans to restructure its seasonal ILI surveillance and continue its virtual clinicians' network, pneumonia, event-based, mortality, virological and vaccine adverse event surveillance. In the UK, pandemic influenza data will be reported using a recently developed web-based informatics portal. In addition to the usual seasonal surveillance elements, new schemes will be added such as data on persons receiving antiviral treatment at dedicated distribution facilities, antimicrobial susceptibility testing, molecular diagnostics testing and real-time modelling. Work is ongoing to increase capacity for both real-time modelling and more frequent reporting by influenza networks. Daily reporting of modelled and observed data (e.g. rates of ILI/100 000 population) is planned and will be folded into a larger daily report for government ministers that provides information about hospital bed availability and local resilience and events (e.g. school closures, ambulance services, etc.).

Canada plans to reduce and streamline reporting data during the pandemic/mitigation phases and not report actual numbers of cases. Instead surveillance will focus on core monitoring activities including virological surveillance, provincial level influenza activity assessments, some form of all-cause mortality monitoring (options for piloting are under way), antiviral adverse events and vaccine safety. Laboratory testing will be prioritized using population-based sampling and/or targeted investigations. Challenges include the unknown impact that anticipated changes in health-care service delivery (e.g. centralized "flu assessment clinics") will have on collection of surveillance data and the variations in data collection/management systems across public health institutions and laboratories at the provincial and territorial levels.

During the plenary discussion, the United States of America indicated that it planned to move from reporting "case counts" during a pandemic to reporting rates of hospitalization for respiratory illness as an example of one of several indicators that are being developed.

Sentinel systems developed since H5N1:

Cambodia and Turkey have reported both human and animal cases of H5N1 influenza. They described how surveillance is currently undertaken amidst the continued threat of H5N1.

Disease surveillance in Cambodia is both passive and active and comprises several components. Passive surveillance for 12 diseases is undertaken at all government health facilities using a syndromic approach, although an evaluation in 2005 documented that completeness of reporting and regular, timely analyses were lacking. Two additional passive approaches are village-based event surveillance in humans for which 29 ,000 village volunteers have been trained and hotlines established for human disease and elevated poultry deaths. Active sentinel surveillance occurs at three levels: outpatient, inpatient and community. However, participation in these schemes is limited: four outpatient clinics undertake active ILI surveillance, two hospitals survey for acute lower respiratory illness (ALRI) and 25 convenience sample villages in one province (~20,000 population) are visited weekly to detect febrile illness and collect specimens for testing.

The Pasteur Institute of Cambodia has received funding from CDC to study the epidemiology of seasonal influenza including an assessment of seasonality, incidence and hospitalization rates, risk factors for severe outcomes and an estimation of influenza-related deaths. Although an existing network of active sentinel sites, coupled with in-country virological capacity, offers the potential for surveillance during a pandemic, many challenges can be anticipated related to the overwhelming burden on health-care systems and the uncertainty of adequate staffing.

Since the appearance of H5N1 human cases in Turkey in early 2006, the country has established surveillance for upper respiratory infection symptoms and "flu like" symptoms in 10 health centres in each of its 14 provinces. "Special vigilance" occurs among schoolchildren and other risk groups. Specimens are obtained and tested for influenza A and B viruses. The current system could be used during a pandemic; during inter-pandemic periods, consideration is being given to integrating other emerging infections.

5.4 Other surveillance systems

Polio:
The polio surveillance network operates using an infrastructure based on:

i) norms and standards, e.g. standard case definitions and investigation procedures;

ii) operational and technical guidance, e.g. laboratory testing and reporting procedures;

iii) networks, e.g. a global laboratory network of 145 laboratories;

iv) human resources: > 3 300 funded professionals and support staff; and

v) physical assets, e.g. vehicles, cells and satellite phones.

The polio surveillance network has been used as a framework to support core capacity for surveillance of other diseases such as measles, rubella and yellow fever. It has also supported the GOARN for various infectious disease outbreaks such as SARS, avian influenza and Ebola, and natural disasters, e.g. the south-east Asia tsunami and the Pakistan earthquake.

Participants agreed that polio surveillance networks could be of potential use during an influenza pandemic: they have national reach and capacity, can identify trigger events, investigate outbreaks and have vast experience in supporting rapid interventions. Optimal use of the polio network during a pandemic would require a case or event definition, a process for investigation and reporting (including linkages with laboratory-based and other relevant networks) and a clear line of communication to those responsible for management of pandemic events.

Chaotic events:
Experience has demonstrated that reliable surveillance can be established quickly in chaotic situations. Surveillance in such settings works best with a simple system developed in advance. One option is the establishment of sentinel sites that are activated when an "alert level" is reached. Key features of the surveillance system are a standardized case definition, a specified frequency and mechanism for reporting (including zero reporting), a person/agency in charge and a mechanism for feedback to reporters. To be workable in a field situation, the case definition should be based on clinical and/or epidemiological criteria and not require laboratory or other diagnostic testing (e.g. radiographic findings). If laboratory confirmation is necessary, e.g. to test samples of ill persons at the beginning and the apparent end of an outbreak, clear objectives and Standard Operating Procedures should be developed and distributed to surveillance and health staff.

Morbidity and mortality estimates are critical during chaotic events and require reliable estimates of the population – both residents and

displaced persons. The fluid nature of the situation necessitates regular updating of denominator data and cross-referencing with more than one source to avoid under- or over-estimations of the population. Typically, rates are stratified into two age groups: < 5 years and ≥ 5 years.

Other challenges in conflict situations include verification of information, integration within national data while minimizing "double case counting" and the definition of staff roles and responsibilities.

6. Other tools and approaches to analyse data during and/or after a pandemic

Modelling and antigenic cartography are two examples of innovative tools that rely on good quality epidemiological and virological surveillance data and can be used to extend observational information.

6.1 Real-time modelling

Real-time modelling aims to provide possible outcomes of an influenza pandemic by integrating experience from previous pandemics, other countries' experience of a new pandemic, national surveillance data and other relevant information. Modelling, by supplementing surveillance systems (which may be compromised during a pandemic), can assist in planning, resource allocation, and policy- and decision-making at national/regional levels. For example, modelling can be used to project where and when the pandemic peak will occur, the number of cases and deaths, whether control measures are working and whether supplies of antivirals and the level of health-care services are adequate.

Modelling during a pandemic will be challenging because the fundamental characteristics of the new virus are unknown and delays in reporting in surveillance systems will need to be taken into account. Consequently, there will be uncertainty in the various parameters used in the model; parameter estimates, however, can be updated as new information becomes available. In addition, models can be developed and tested in advance of the pandemic. There are major educational and communication challenges to clarify for policy-makers and the public about the distinction between modelled estimates/projections and observed data.

6.2 Antigenic cartography

This novel methodology combines antigenic, genetic and epidemiologic data to help explain global patterns of influenza virus strain circulation. For the last few years, antigenic cartography has been used as an adjunct to standard methods for selecting the vaccine strains for the northern and southern hemispheres. Analyses to date suggest that new influenza virus antigenic variants emerge more often from east and southeast Asia and subsequently seed the rest of the world. If data could be made available in real time during a pandemic, antigenic cartography may be able to help forecast pandemic trends and virus circulation.

7. Key issues for surveillance of pandemic influenza

During the deliberations of the break-out groups and discussions in plenary sessions, the following key issues and challenges emerged that will require further consideration by the working group.

7.1 Changing information needs during a pandemic

Changing priorities related to data collection and analysis need to be considered when planning for pandemic surveillance at national and global levels (Figure 1). At the beginning of the pandemic, evaluation of the initial cases will be important to determine critical epidemiological, clinical and virological characteristics

of the pandemic virus. Such information will help WHO and countries refine their preparedness strategies and plans. Priority information includes:

- epidemiological parameters such as the reproductive number (R_0), intergeneration time, incubation period and risk factors for infection;
- patient-level data such as the spectrum of clinical disease, case–fatality rates, hospitalization rates, duration of hospitalization and efficacy of antiviral agents for treatment and prophylaxis;
- population-level data about the utility of public health measures such as quarantine and school closures to reduce transmission; and
- virological data such as resistance to antiviral agents and performance of diagnostic tests.

Standardized approaches to collect detailed data will facilitate aggregation or intercountry comparisons.

As the pandemic progresses, it will not be possible to sustain detailed data collection at global and national levels for individual cases. Nonetheless, it will be necessary to re-examine many of the parameters outlined above at various intervals throughout the pandemic, as the pandemic begins in new countries as well as the end of the pandemic to assess the evolution of the virus.

Triggers to move from case-based to aggregated reporting need to be delineated. During the pandemic, consistent reporting to WHO of core surveillance information from as many countries as possible will be important to monitor global epidemiological trends and characteristics, as well as the pandemic's impact and country responses. Post-pandemic information needs are likely to include emphasis on research and modelling and identification of important lessons.

7.2 Identification of core global data

One of the principal objectives of the consultation was to determine the core information that countries could provide WHO to help monitor and manage a pandemic at the national level. During break-out group discussions (Annex 4) participants generally agreed that a WHO web site should report, as a minimum, information on the geographic spread of the pandemic, country level activity (e.g. increasing/decreasing/no change or high/medium/low), characteristics of the virus (e.g. antiviral resistance) and country-specific public health actions (e.g. border closures). Additional data such as the number of cases and deaths would be desirable, although the feasibility of providing such information was considered unlikely.

7.3 Distinguishing surveillance from other activities

During the consultation, participants advocated for WHO's facilitation of information and data collection activities beyond traditional public health surveillance that focuses on measures of time, place and person, including

- detailed case investigations or special studies such as on the first few hundred cases;
- recommendations and guidance;
- periodic updates or distillations of available information about clinical, epidemiological and virological features of the pandemic virus;
- the effectiveness of pharmaceutical and non-pharmaceutical measures;
- a narrative summary or historical account and timeline of the evolution and global spread of the pandemic; and
- modelling and other innovative data tools.

7.4 Clearly defined objectives and processes

The boundaries of public health surveillance can become blurred, especially in the setting of concurrent data collection activities by and for multiple stakeholders. Accordingly, plenary speakers and participants emphasized the importance of establishing clear objectives, definitions, processes and procedures for pandemic influenza surveillance and reporting. Several participants indicated the need for practical guidance on conducting surveillance during a pandemic as well as guidance on the coordination and standardization of information collected during case investigations and special studies. The role of virological testing and how testing strategies might change during a pandemic also needed to be addressed.

7.5 Surveillance methodologies

Plenary presentations and discussions reinforced the fact that seasonal influenza surveillance and plans for pandemic surveillance range from complex, multi-component strategies to none at all. Surveillance in chaotic situations and the adaptation of "platforms such as the polio network and IDS are other approaches. It was agreed that it is not possible or reasonable to expect countries to conform to a uniform global system of surveillance during a pandemic. However, identifying approaches and tools that can overlay all systems and permit monitoring at a global level is critical.

7.6 Dissemination of information

In a rapidly evolving situation such as a pandemic with different information needs and stakeholders, open and transparent access to data are essential. One of the basic ways that global surveillance information will be shared is via WHO's web site. Participants envisioned a site that is simple, visual and intuitive (Annex 4). Access to data was raised as a separate but related issue. One of the lessons learnt during the SARS outbreak was the need to ascertain WHO's role as the custodian of a global dataset. A data management plan outlining what information can be shared, with whom, under which situations and the mechanisms for doing so should be discussed with countries in advance of a pandemic.

7.7 Setting out realistic expectations

The demands of a pandemic will be overwhelming, even for well-resourced countries. Participants agreed that it would be prudent to inform stakeholders including the media, politicians, academics and the public in advance of a pandemic on the surveillance information that will be available as well as its limitations. The feasibility and sustainability of pandemic surveillance given reduced staffing, overwhelmed health-care and public health systems and possible social and infrastructure disruption, were also raised.

World Health Organization

WHO Consultation on Surveillance for Pandemic Influenza
10 - 12 December 2007 - Geneva, Switzerland

AGENDA

Day 1: Monday, 10 December 2007, Salle A

08:30 - Registration
09:00

09:00 Opening
09:30

Welcome/opening remarks - *D. Heymann*

Nomination of Chairperson and Rapporteur

Adoption of provisional agenda and programme

09:30 - Session 1: Introduction of the frame of discussion
10:30

Pandemic surveillance scope and usefulness - *K. Fukuda*

Historical background on pandemics - gaps in knowledge - *A. Nicoll*

Lessons learned from SARS outbreak regarding surveillance at global level - *A. Merianos*

Discussion

10:30 - Refreshment Break
11:00

11:00 - Session 2: Presentation of the different perspectives
12:30

Expectation from countries - What do they want to know at global level to better address national concerns - *M. Van der Sand, E. Coker, E. Zavala, J. Kwon, M. Gouya*

Discussion *(Facilitator J. Watson)*

12:30 - Lunch Break
14:00

14:00 - Session 2: Presentation of the different perspectives (continued)
15:15

Surveillance data in the public domain: informing the public, communicating risk and managing rumours. *J. Rainford, J. Gale, H. Branswell*

Surveillance during pandemic and International Health Regulations, *B. Plotkin*

15:15 - Session 3: Development of a list of core information.
15:30

Current surveillance data at global level - *J. Fitzner*

Introduction to work in break out groups - *S. Briand*

15:30 - Refreshment Break
16:00

16:00 - Break out Group Discussion (Room M205, Salle G and Salle A)
17:30

18:30 - Welcome Cocktail at WHO Main Building Cafeteria
19:30

Day 2: Tuesday, 11 December 2007, Salle A

09:00 - Session 3: Development of a list of core information
10:30 (continued)

Feed back from work groups

10:30 - Refreshment Break
11:00

11:00 - Session 4: Review if existing surveillance systems are
12:30 adapted for a pandemic situation -what are the options?

Long-standing influenza surveillance systems: options for pandemic situation - *K. Taniguchi, J. Watson, J. Macey*

Newly created surveillance systems since H5N1 appeared - options for pandemic situation - *S. Vong, O. Ergonul*

Discussion *(facilitator O. Mansoor)*

12:30 - 14:00 **Lunch Break**

14:00-15:30 **Session 5: Review other approaches to gather/analyse information during a pandemic**

Complementary sources of information - *S. Vaux*

Lessons learned in setting up ad hoc surveillance system in chaotic situation - *M. Henkens*

Antigenic cartography - *C. Russell*

The polio surveillance network and process - *C. Maher*

Discussion

15:30 - 16:00 **Refreshment Break**

16:00 - 17:30 **Session 6: Explore innovative tools during a pandemic - role of real-time modelling**

Real time modelling what are the benefits and the data requirements - *N. Gay*

Discussion *(Facilitator L. Wolfson)*

Day 3: Wednesday, 12 December 2007, Salle C

9:00 - 10:00 **Session 7: Flow of information: interaction between levels.**

Experience of an intermediate level- *J. Paget, W. Alemu*

Discussion *(Facilitator K. Fukuda)*

10:00 - 10:30 **Session 8: To define type of global information dissemination.**

Proposal of global information dissemination to be discussed in break out groups - *K. Vandemaele*

10:30 - 11:00 **Refreshment Break**

11:00 - 12:30 **Session 8 (continued)**

Break out groups (Salle C, Room M105, Room M605)

12:30 - Lunch Break
13:30

13:30 - Session 8: (continued)
14:00
Review of comments and recommendations from groups

14:.00 - Session 9: Summary of discussions from session 1 to 8
15:00 *(Facilitator S. Briand)*

15:00 - Refreshment Break
15:30

15:30 - Session 10: To define the role of the working group who will
16:30 finalize the manual for global pandemic surveillance

Organized discussion *(Facilitator S. Briand)*

- Revision of term of reference
- Revision of time line

16:30 - Closure
17:00

Annex 2. Participants

WORLD HEALTH ORGANIZATION

WHO Consultation on Surveillance for Pandemic Influenza
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ANNEX 3. Development of a list of core information

Three break-out groups considered what core information would be used at the beginning, during and after a pandemic. Each group was given a different scenario that detailed how long the pandemic had been under way, the number of global cases and whether "their" country had been affected. All groups organized their data into four general categories: information about the disease, disease control measures, descriptive epidemiology, and other information.

The group reports are summarized below.

Information needs at the beginning, during and after an influenza pandemic

	Time during pandemic			Comments
	Start Group 1	During Group 2	After Group 3	
Information on the disease				
Clinical features at initial presentation, evolution/course over time, laboratory results, complications, morbidity/ mortality/other outcomes	x	x	x	Complications include secondary bacterial infections and recommended therapy.
Incubation period	x			
Spectrum of disease including asymptomatic infection	x	x	x	What is the role of sub-clinical infection in disease transmission?
Pathology			x	
Clinical management guidance		x	x	
Period of infectivity and risk to others	x	x		
Evidence of selective immunity in some persons		x		Information may be helpful to "retool" the vaccine.
Diagnostic tests	x	x		Which tests should be used, when, what is their sensitivity/specificity?
Characteristics of the virus				
• Period of shedding	x	x		
• Environmental survival			x	
• Antigenic/genetic change over time			x	
• Other circulating viruses			x	
• Vaccine-induced selection pressure			x	
• Post-pandemic circulation and vaccine strain selection			x	

	Time during pandemic			Comments
	Start Group 1	During Group 2	After Group 3	
Disease control measures				
Antivirals				
• Effectiveness	x	x	x	Clinical and genetic. When to administer, optimal dose. Availability from WHO.
• Development of resistance	x	x		
• Use for prophylaxis	x	x		
• General guidance	x			
• Availability and projected needs	x	x		
Vaccine				
• Effectiveness	x	x	x	Including effectiveness of H5 vaccine.
• Status of vaccine development		x		
• Adverse events		x		
• Availability and projected needs	x			
Non-pharmaceutical interventions				
• Effectiveness	x		x	Including travel restrictions, border closures, school closures.
Hospital utilization/impact				
• In-patient admissions	x			Number of severe cases.
• Out-patient attendance	x			
• Intensive care unit admissions	x			
• Non-influenza services			x	
Infection control measures				
• Effectiveness in hospitals	x			
• Personal protective equipement (PPE) availability and projected needs	x			
• PPE recommendations		x		
Diagnostic reagents	x			Availability and projected needs.
Effectiveness of combination measures			x	
Operational issues			x	Implementation ability, timing.
Economic impact of control measures			x	Identify key indicators.
Social disruption related to control measures			x	Identify key indicators.
Vaccine strategies			x	Feasibility/effectiveness.

	Time during pandemic			Comments
	Start Group 1	During Group 2	After Group 3	
Descriptive epidemiology				
Age and gender	x	x	x	
Attack rates	x		x	Age-specific; household; occupational.
Serial/generation interval	x			
R_o			x	
Risk groups/identifiable risk factors for infection	x	x	x	Persons (e.g. pregnant women, certain occupations) and settings (e.g. hospitals, schools, public transport) at increased risk.
Geographic distribution/spread	x	x	x	Including projections for future and distribution of mortality.
Influenza mortality rates /Case fatality rate (CFR))	x	x	x	Age-stratified.
Non-influenza morbidity/mortality			x	
Patterns of disease (e.g. CFR)	x	x		Changes over time, differences by country (e.g. due to differences in case definitions, surveillance methods, evolution of virus).
Shape of epidemic curve		x		How countries can gauge where they are relative to peak.
Additional waves	x	x	x	Likelihood and severity.
Other				
WHO recommendations (e.g. containment of first cases/clusters; how to conduct surveillance; should country borders be closed)	x	x		WHO's response to countries that do not follow WHO guidance.
WHO reporting requirements	x			
WHO policy changes	x			Including justification
WHO leadership assessment			x	At all levels
WHO support staff		x		Availability to assist countries
Case definitions	x	x		Changes over time; differences by country
Risk communications	x	x	x	Advice, information packs, effectiveness
Narrative account	x			Including why containment failed (if relevant), rapidity of spread to other countries, why key events occurred, how and why critical public health decisions were made.
Peak levels of absenteeism		x	x	
Disposal of bodies		x		
Triggers for scaling back response		x		

	Time during pandemic			Comments
	Start Group 1	During Group 2	After Group 3	
How to ship specimens internationally		x		
Overall economic impact			x	Gross Domestic Product (GDP), affected industries, breakdown of central services.
Coping capacities of countries			x	
Transmission to and from animals			x	

ANNEX 4. Development of a global pandemic web-based report

Sharing of information at the global level will be very important during a pandemic. In five separate break-out groups, participants considered a number of issues including:

- What is the minimum information common to all and meaningful to describe either qualitatively or quantitatively aspects of the pandemic such as its geographical spread, severity and intensity?
- How frequently should this information be posted?
- What level of detail should be displayed?
- What is feasible for countries during the chaos of a pandemic?

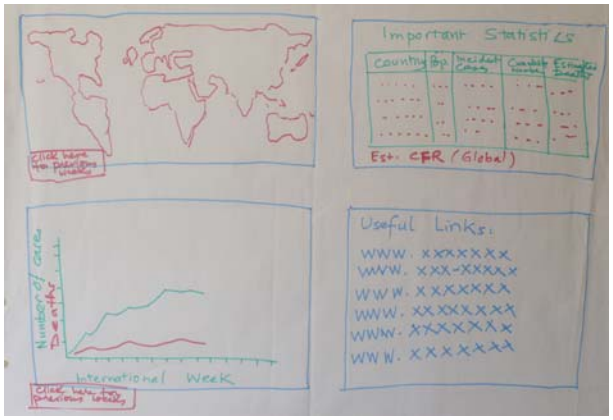
Common themes

Several common themes emerged during the break-out group discussions:

- All groups envisioned that WHO would post global data visually using a world map. Country-level pandemic influenza activity/severity (e.g. increasing/decreasing/no change/no report) could be indicated using a colour-coding scheme. Most groups indicated a weekly reporting frequency. One group suggested that it would be helpful to be able to link to the previous week's map to allow for week-to-week comparisons.
- All groups indicated that individual country data should be available as well. Four of the five groups envisioned access to country-specific data by "clicking on" an individual country on the world map; the fifth group organized country-specific data in tabular format. Groups had varying expectations, however, about the level of country-specific detail that should be available; three of the groups included information about country-specific public health actions that might have global impact (e.g. border or airport closures).
- Two groups indicated that regional-level and sub-national level of data should also be presented or available.
- One group organized cases as confirmed/probable/suspected.
- Most groups indicated that updated virological information should be included on the web site; antiviral resistance was uniformly cited.
- Several groups included epidemic curves (either at global or national levels), typically of cases and/or deaths and stratified by age if possible.

The following is a visual outline of elements that the break-out groups considered should be included in the WHO influenza pandemic web site.

Break-out group sketch of a WHO pandemic web site



Monitoring disease severity

One group proposed that each country should identify a small number of sentinel hospitals to help monitor disease severity. On a weekly basis each hospital would report the total number of hospitalizations, the proportion due to respiratory disease, the total number of deaths and the proportion that were respiratory-related.

Information synthesis

In addition to global and national surveillance data, one group proposed that the WHO pandemic web site include a detailed section on the "Current State of Knowledge on the Pandemic Virus". This section would be developed before the pandemic and updated during the pandemic based on a synthesis of all available information to date, with the understanding that such information may not be complete but the "best available". The information for this section would be derived from investigations of clusters of initial cases or other special studies. Specific topics included:

- Epidemiologic features
  - Incubation period
  - Modes of transmission
  - Period of communicability
  - Occupations of cases
  - Clinical attack rates
- Clinical features
  - Presentation and progression
  - Symptomatic period
  - Response to supportive therapy and treatment
  - Secondary complications (rates of viral and bacterial pneumonia; severity, treatment, drug-resistance; other complications)
- Clinical severity indicators
  - Hospitalization rate
  - Ventilator use
  - Delayed effects of infection such as long-term respiratory or neurological impairment
- Recommended laboratory specimens and observed performance of diagnostic tests
  - Laboratory testing (optimal specimens and diagnostic methods)
  - Strain characterization
- Antivirals
  - Treatment recommendations (e.g. use, timing)
  - Observed effectiveness
  - Resistance
  - Adverse events
- Vaccines
  - Level of match or cross-protection
  - Observed effectiveness
  - Adverse events.

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WHO/HSE/GIP/2009.1